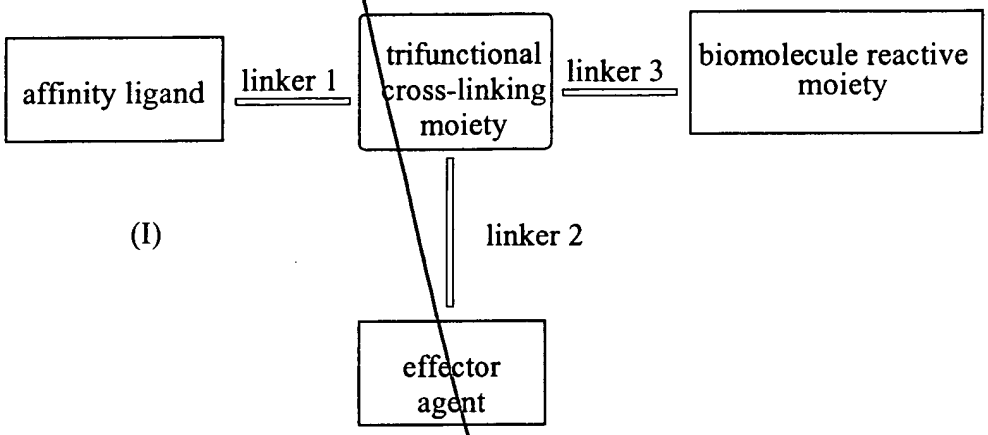
CLEAN COPY OF THE AMENDED AND NEW CLAIMS

1. (Amended) Reagent for conjugation to a biomolecule for diagnosis and treatment of human and animal conditions or diseases, wherein the reagent is a single molecule with at least three functional parts and has the following schematic structure (I):



(I)

a) wherein a trifunctional cross-linking moiety is coupled to

b) an affinity ligand via a linker 1, said affinity ligand being capable of binding with another molecule having affinity for said ligand which is stabilized towards cleavage by biotinidase of the biotinamide bond to release biotin, to

c) an effector agent, optionally via a linker 2, said effector agent exerting its effect on cells, tissues and/or humorous molecules in vivo or ex vivo, and to

d) a biomolecule reactive moiety, optionally via a linker 3, said moiety being capable of forming a bond between the reagent and the biomolecule.

2. (Amended) Reagent according to claim 1, wherein the trifunctional cross-linking moiety is selected from the group consisting of triaminobenzene, tricarboxybenzene, dicarboxyaniline and diaminobenzoic acid.

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6. (Twice Amended) Reagent according to claim 1, wherein the biotin derivative is selected from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, desthiobiotin, diaminobiotin, biotin sulfoxide, and biotin sulfone, or other molecules thereof that having essentially the same binding function.

7. (Amended) Reagent according to claim 5, wherein the stability towards enzymatic cleavage of the biotinamide bond to release biotin has been improved by using norbiotin or homobiotin.

Sub D' Cont

8. (Twice Amended) Reagent according to claim 1, wherein linker 1 serves as an attaching moiety and a spacer between the trifunctional cross-linking moiety and the biotin moiety such that binding with avidin or streptavidin, or any other derivatives, mutants or fragments of avidin or streptavidin having essentially the same binding function to the affinity ligand, is not sterically hindered.

9. (Twice Amended) Reagent according to claim 1, wherein linker 1 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization of the biotin moiety.

10. (Amended) Reagent according to claim 1, wherein stability towards enzymatic cleavage of the biotinamide bond to release biotin has been improved by introducing an alpha carboxylate or an N-methyl group in linker 1.

Sub D' Cont

11. (Amended) Reagent according to claim 1, wherein the effector agent is selected from the group consisting of synthetic toxins, natural occurring toxins, enzymes capable of converting a pro-drug to an active drug, immunosuppressive agents, immunostimulating agents, and radionuclide binding/bonding moieties, with or without the radionuclide.

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14. (Twice Amended) Reagent according to claim 1, wherein the effector agent comprises aryl halides and vinyl halides for radionuclides of halogens, amino-carboxy derivatives, and cyclic amines for In, Y, Pb, Bi, Cu, Sm, and Lu radionuclides.

Sub D' Cont

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15. (Twice Amended) Reagent according to claim 1, wherein the effector agent is provided with positron imaging radionuclides, therapeutic radionuclides, and gamma imaging radionuclides.

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17. (Twice Amended) Reagent according to claim 1, wherein linker 2 provides a spacer length of 1-25 atoms or groups of atoms.

Sub D' Cont

18. (Twice Amended) Reagent according to claim 1, wherein linker 2 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization.

19. (Twice Amended) Reagent according to claim 1, wherein the biomolecule reactive moiety is selected from the group consisting of active esters, aryl or alkyl imidates, alkyl or aryl isocyanates or isothiocyanates reactive with amino groups on the biomolecule, maleimides or alpha-haloamides reactive with sulfhydryl groups on the biomolecule, aryl and alkylhydrazines or alkyl or aryl hydroxylamines reactive with aldehyde or ketone groups naturally occurring or synthetically produced on the biomolecule.

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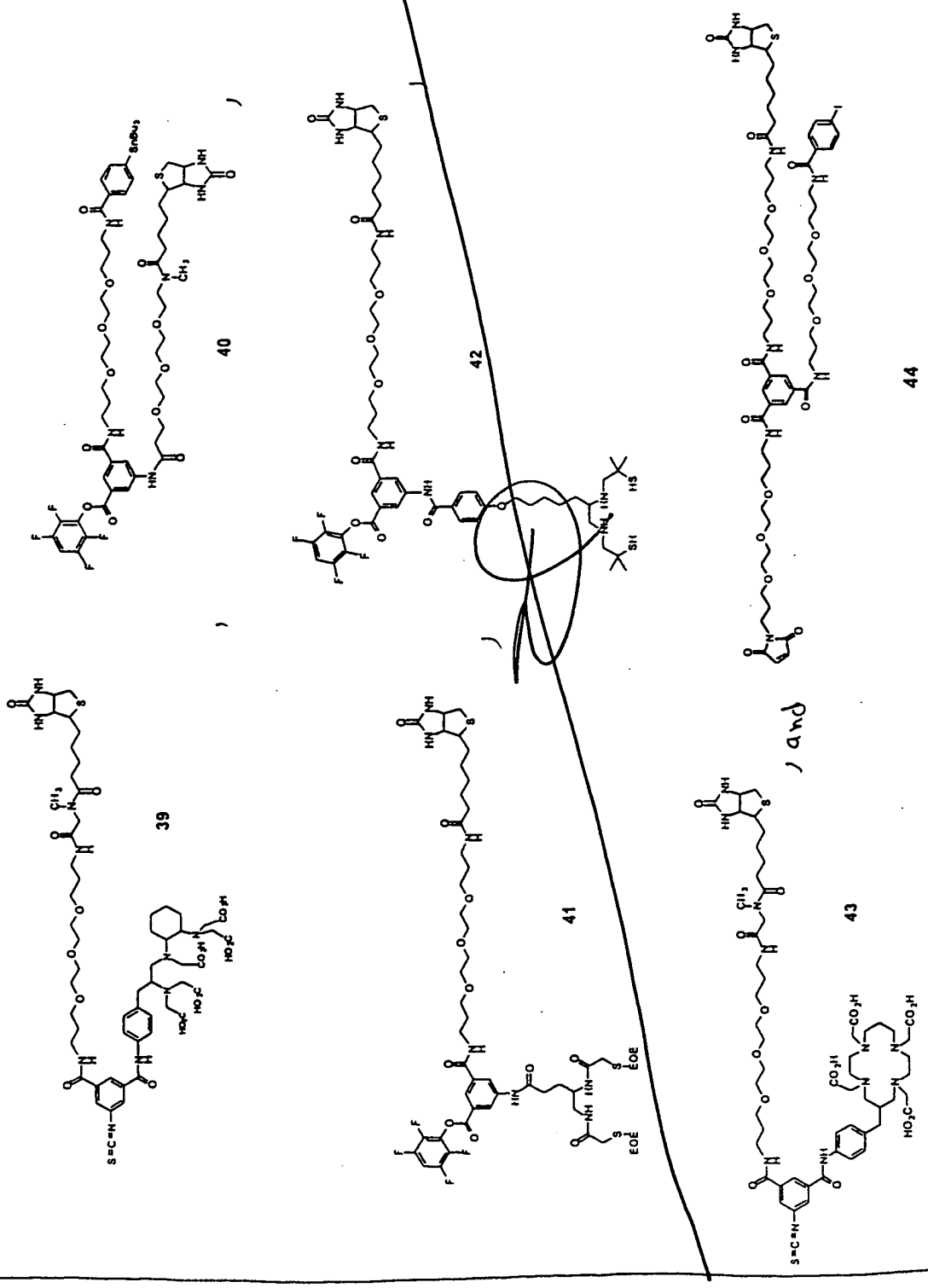
Sub D' Cont

21. (Twice Amended) Reagent according to claim 1, wherein linker 3 provides a spacer of a length of 1-25 atoms or groups of atoms.

22. (Twice Amended) Reagent according to claim 1, wherein linker 3 contains hydrogen bonding atoms, or ionizable groups to aid in water solubilization.

23. (Twice Amended) Reagent according to claim 1 wherein it is selected from the group consisting of the following compounds:



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, and

26. (Amended) Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to claim 1 is conjugated to a biomolecule, and wherein said conjugated is added to the blood circulation of a mammal and kept therein for a certain of time in order to be concentrated to the target tissue or cells, wherein the biomolecules not being attached to the target tissue are completely or partially removed from the blood circulation by administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

27. (Amended) Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to claim 1 provided with a radionuclide is conjugated to a biomolecule, or alternatively, the reagent is conjugated to the biomolecule prior to attachment of the radionuclide, and the said radioactive conjugated biomolecule is added to the blood circulation of a mammal and kept therein for a certain period of time in order to be concentrated to the target tissue or cells, wherein the biomolecules that are not being attached to the target tissue are completely or partially removed from the blood circulation by administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

28. (Amended) Kit for extracorporeally eliminating or at least reducing the concentration of a non-tissue-bound therapeutic or diagnostic biomolecule conjugate, which has been introduced to a mammalian host and kept therein for a certain time in order to be concentrated to the specific tissues or cells by being attached thereto, in the plasma or whole blood of the vertebrate host, said kit comprising a therapeutic or diagnostic biomolecule, a reagent for simultaneous conjugation of an affinity ligand and an effector agent to a biomolecule, means for extracoporeal circulation of whole blood or plasma from the vertebrate host, an optional plasma separation device for separation of plasma from blood, an extracoporeal adsorption device, and a means for return of whole blood or plasma without or with the remainder of non-tissue-bound target specific therapeutic or diagnostic agent to the

mammalian host, wherein the adsorption device comprises immobilized receptors specific towards an affinity ligand.

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Sub D' Cont

29. (Amended) A kit according to claim 28, wherein the effector agent is selected from the group consisting of synthetic toxins, naturally occurring toxins, enzymes, capable of converting a pro-drug to an active drug, immunosuppressive agents, immunostimulating agents, and radionuclide binding/bonding moieties with or without the radionuclide.

Please add the following new claims:

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31. (New) Reagent according to claim 9, wherein the hydrogen bonding atoms are ethers or thioethers and the ionizable groups are carboxylates, sulfonates, or ammonium groups.

Sub D' Cont

32. (New) Reagent according to claim 14, wherein the amino-carboxy derivatives are EDTA or DTPA derivatives, and the cyclic amines are NOTA,. DOTA, or TETA.

33. (New) Reagent according to claim 32, wherein the DTPA derivatives are Me-DTPA, CITC-DTPA, and cyclohexy;-DTPA.

34. (New) Reagent according to claims 15, wherein the positron imaging radionuclides are selected from the group consisting of F-18, Br-75, Br-76, and I-124, the therapeutic radionuclides are selected from the group consisting of Y-90, I-131, In-114m, Re-186, Re-188, Cu-67, Sm-157, Lu-177, Bi-212, Bi-213, At-211, and Ra-223, and the gamma imaging radionuclides are selected from the group consisting of Tc-99m, In-111 and I-123.

35. (New) Reagent according to claim 17, wherein linker 2 provides a spacer length of 16-18 atoms.

36. (New) Reagent according to claim 18, wherein hydrogen bonding atoms are ethers or thioethers, and the ionizable groups are carboxylates, sulfonates, or ammonium groups.

B'7 Cont'd

37. (New) Reagent according to claim 19, wherein the active esters are selected from the group consisting of N-hydroxy-succinimide esters, sulfo-N-hydroxysuccinimide esters, phenolic esters.

Subj. D' Cont'd

38. (Twice Amended) Reagent according to claim 21, wherein linker 3 provides a spacer of a length of 6-18 atoms.

39. (Twice Amended) Reagent according to claim 22, wherein the hydrogen bonding atoms are ethers or thioethers and the ionizable groups are carboxylates, sulfonates, or ammonium groups.